

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

1. (Original) An anti-CD20 antibody-cytotoxic agent conjugate, wherein the cytotoxic agent of the anti-CD20 antibody-cytotoxic agent conjugate has an  $IC_{50}$  of between 40-fold and 4,000-fold less than the  $IC_{50}$  of doxorubicin, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, and wherein the  $IC_{50}$  of each of the cytotoxic agent and doxorubicin is measured by a method comprising:

- (a) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of the cytotoxic agent for a 72- to 96-hour period;
- (b) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of doxorubicin for a 72- to 96-hour period; and
- (c) identifying a concentration of the cytotoxic agent and doxorubicin, respectively, at which 50% fewer cells in the CD20-expressing cell populations of steps (a) and (b), respectively, are viable at the end of the period relative to a CD20-expressing cell population cultured in the absence of the cytotoxic agent and doxorubicin,

wherein the CD20-expressing cell populations of steps (a), (b) and (c) are of the same cell type and are cultured under the same conditions,

and wherein the concentration of the cytotoxic agent and doxorubicin identified in step (c) is the  $IC_{50}$  of the cytotoxic agent and doxorubicin, respectively.

2-5 (Canceled)

6. (Original) An anti-CD20 antibody-cytotoxic agent conjugate, wherein the anti-CD20 antibody-cytotoxic agent conjugate has an  $IC_{50}$  of between 40-fold and 4,000-fold less than the  $IC_{50}$  of an anti-CD20 antibody-doxorubicin conjugate, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, and wherein the  $IC_{50}$  of each of the anti-CD20 antibody-cytotoxic agent

conjugate and the anti-CD20 antibody-doxorubicin conjugate is measured by a method comprising:

- (a) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of the anti-CD20 antibody-cytotoxic agent conjugate for a 72- to 96-hour period;
- (b) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of the anti-CD20 antibody-doxorubicin conjugate for a 72- to 96-hour period; and
- (c) identifying a concentration of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate, respectively, at which 50% fewer cells in the CD20-expressing cell populations of steps (a) and (b), respectively, are viable at the end of the period relative to a CD20-expressing cell population type cultured in the absence of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate,

wherein the CD20-expressing cell populations of steps (a), (b) and (c) are of the same cell type and are cultured under the same conditions,

and wherein the concentration of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate identified in step (c) is the  $IC_{50}$  of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate, respectively.

7-11 (Canceled)

12. (Original) An anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate has a rate of accumulation in a CD20-expressing cell that is between 20-fold and 5,000-fold greater than the rate of accumulation of an unconjugated form of the anti-CD20 antibody in the CD20-expressing cell, wherein the rates of accumulation of the conjugate and of the unconjugated form of the antibody are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the unconjugated antibody, wherein the populations of steps (a) and (b) are cultured under the same conditions; and

- (c) measuring the amount of the conjugate and unconjugated antibody accumulated in the populations of steps (a) and (b), respectively.

13-17 (Canceled)

18. (Original) An anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate has a rate of accumulation in a CD20-expressing cell that is between 20-fold and 5,000-fold greater than the rate of accumulation of an anti-CD20 antibody-doxorubicin conjugate in a CD20-expressing cell of the same cell type, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, and wherein the rates of accumulation of the anti-CD20 antibody-cytotoxic agent conjugate and of the anti-CD20 antibody-doxorubicin conjugate are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-cytotoxic agent conjugate;
- (b) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-doxorubicin conjugate, wherein the populations of steps (a) and (b) are cultured under the same conditions; and
- (c) measuring the amount of the anti-CD20 antibody-cytotoxic agent conjugate and anti-CD20 antibody-doxorubicin conjugate accumulated in the populations of steps (a) and (b), respectively.

19-21 (Canceled)

22. (Original) An anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate exhibits an accumulation in a non-peripheral region inside a CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of an unconjugated form of the anti-CD20 antibody in the CD20-expressing cell, wherein the accumulation of the conjugate and of the unconjugated form of the antibody are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the unconjugated form of the anti-CD20 antibody; and

- (c) detecting by confocal fluorescence microscopy localization of the conjugate and the unconjugated form of the anti-CD20 antibody in the populations of steps (a) and (b), respectively,

wherein the populations of steps (a) and (b) are cultured under the same conditions and for the same period of time, and wherein the conjugate exhibits an accumulation in the CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of the unconjugated form of the anti-CD20 antibody in the CD20-expressing cell if:

- (i) between 1.5-fold and 5,000-fold as many cells of the population of step (a) contain a detectable amount of the conjugate in a non-peripheral region as the number of cells of the population of step (b) contain the unconjugated form of the antibody in a non-peripheral region; or
- (ii) the accumulation of the conjugate in a non-peripheral region of the majority of CD20-expressing cells of the population of step (a) is between 1.5-fold and 5,000-fold greater than the accumulation of the unconjugated form of the anti-CD20 antibody in the majority of CD20-expressing cells of the population of step (b).

23-25 (Canceled)

26. (Original) An anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate exhibits an accumulation in a non-peripheral region inside a CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of an anti-CD20 antibody-doxorubicin conjugate, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, in the CD20-expressing cell, wherein the accumulation of the conjugate and of the anti-CD20 antibody-doxorubicin conjugate are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-doxorubicin conjugate; and
- (c) detecting by confocal fluorescence microscopy localization of the conjugate and the anti-CD20 antibody-doxorubicin conjugate in the populations of steps (a) and (b), respectively,

wherein the populations of steps (a) and (b) are cultured under the same conditions and for the same period of time, and wherein the conjugate exhibits an accumulation in the CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of the anti-CD20 antibody-doxorubicin conjugate in the CD20-expressing cell if:

- (i) between 1.5-fold and 5,000-fold as many cells of the population of step (a) contain a detectable amount of the conjugate in a non-peripheral region as the number of cells of the population of step (b) contain the anti-CD20 antibody-doxorubicin conjugate in a non-peripheral region; or
- (ii) the accumulation of the conjugate in a non-peripheral region of the majority of CD20-expressing cells of the population of step (a) is between 1.5-fold and 5,000-fold greater than the accumulation of the anti-CD20 antibody-doxorubicin conjugate in the majority of CD20-expressing cells of the population of step (b).

27-64            (Canceled)

65.            (Original) A pharmaceutical composition comprising an anti-CD20 antibody-cytotoxic agent conjugate, wherein the cytotoxic agent of the anti-CD20 antibody-cytotoxic agent conjugate has an  $IC_{50}$  of between 40-fold and 4,000-fold less than the  $IC_{50}$  of doxorubicin, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, and wherein the  $IC_{50}$  of each of the cytotoxic agent and doxorubicin is measured by a method comprising:

- (a)    culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of the cytotoxic agent for a 72- to 96-hour period;
- (b)    culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of doxorubicin for a 72- to 96-hour period; and
- (c)    identifying a concentration of the cytotoxic agent and doxorubicin, respectively, at which 50% fewer cells in the CD20-expressing cell populations of steps (a) and (b), respectively, are viable at the end of the period relative to a CD20-expressing cell population cultured in the absence of the cytotoxic agent and doxorubicin,

wherein the CD20-expressing cell populations of steps (a), (b) and (c) are of the same cell type and are cultured under the same conditions,  
and wherein the concentration of the cytotoxic agent and doxorubicin identified in step (c) is the IC<sub>50</sub> of the cytotoxic agent and doxorubicin, respectively.

66. (Original) A pharmaceutical composition comprising an anti-CD20 antibody-cytotoxic agent conjugate, wherein the anti-CD20 antibody-cytotoxic agent conjugate has an IC<sub>50</sub> of between 40-fold and 4,000-fold less than the IC<sub>50</sub> of an anti-CD20 antibody-doxorubicin conjugate, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, and wherein the IC<sub>50</sub> of each of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate is measured by a method comprising:

- (a) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of the anti-CD20 antibody-cytotoxic agent conjugate for a 72- to 96-hour period;
- (b) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of the anti-CD20 antibody-doxorubicin conjugate for a 72- to 96-hour period; and
- (c) identifying a concentration of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate, respectively, at which 50% fewer cells in the CD20-expressing cell populations of steps (a) and (b), respectively, are viable at the end of the period relative to a CD20-expressing cell population cultured in the absence of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate,

wherein the CD20-expressing cell populations of steps (a), (b) and (c) are of the same cell type and are cultured under the same conditions,

and wherein the concentration of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate identified in step (c) is the IC<sub>50</sub> of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate, respectively.

67. (Original) A pharmaceutical composition comprising an anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate has a rate of accumulation in a CD20-expressing cell that is between 20-fold and 5,000-fold greater than the rate of accumulation of an unconjugated form of the anti-CD20 antibody in the CD20-expressing cell, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the rates of accumulation of the conjugate and of the unconjugated form of the antibody are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the unconjugated antibody, wherein the populations of steps (a) and (b) are cultured under the same conditions; and
- (c) measuring the amount of the conjugate and unconjugated antibody accumulated in the populations of steps (a) and (b), respectively.

68. (Original) A pharmaceutical composition comprising an anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate has a rate of accumulation in a CD20-expressing cell that is between 20-fold and 5,000-fold greater than the rate of accumulation of an anti-CD20 antibody-doxorubicin conjugate in a CD20-expressing cell of the same cell type, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, and wherein the rates of accumulation of the anti-CD20 antibody-cytotoxic agent conjugate and of the anti-CD20 antibody-doxorubicin conjugate are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-cytotoxic agent conjugate;
- (b) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-doxorubicin conjugate, wherein the populations of steps (a) and (b) are cultured under the same conditions; and
- (c) measuring the amount of the anti-CD20 antibody-cytotoxic agent conjugate and anti-CD20 antibody-doxorubicin conjugate accumulated in the populations of steps (a) and (b), respectively.

69. (Original) A pharmaceutical composition comprising an anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate exhibits an accumulation in a non-

peripheral region inside a CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of an unconjugated form of the anti-CD20 antibody in the CD20-expressing cell, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the accumulation of the conjugate and of the unconjugated form of the antibody are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the unconjugated form of the anti-CD20 antibody; and
- (c) detecting by confocal fluorescence microscopy localization of the conjugate and the unconjugated form of the anti-CD20 antibody in the populations of steps (a) and (b), respectively,

wherein the populations of steps (a) and (b) are cultured under the same conditions and for the same period of time, and wherein the conjugate exhibits an accumulation in the CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of the unconjugated form of the anti-CD20 antibody in the CD20-expressing cell if:

- (i) between 1.5-fold and 5,000-fold as many cells of the population of step (a) contain a detectable amount of the conjugate in a non-peripheral region as the number of cells of the population of step (b) contain the unconjugated form of the antibody in a non-peripheral region; or
- (ii) the accumulation of the conjugate in a non-peripheral region of the majority of CD20-expressing cells of the population of step (a) is between 1.5-fold and 5,000-fold greater than the accumulation of the unconjugated form of the anti-CD20 antibody in the majority of CD20-expressing cells of the population of step (b).

70. (Original) A pharmaceutical composition comprising an anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate exhibits an accumulation in a non-peripheral region inside a CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of an anti-CD20 antibody-doxorubicin conjugate, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, in the CD20-expressing cell, wherein the



accumulation of the conjugate and of the anti-CD20 antibody-doxorubicin conjugate are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-doxorubicin conjugate; and
- (c) detecting by confocal fluorescence microscopy localization of the conjugate and the anti-CD20 antibody-doxorubicin conjugate in the populations of steps (a) and (b), respectively,

wherein the populations of steps (a) and (b) are cultured under the same conditions and for the same period of time, and wherein the conjugate exhibits an accumulation in the CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of the anti-CD20 antibody-doxorubicin conjugate in the CD20-expressing cell if:

- (i) between 1.5-fold and 5,000-fold as many cells of the population of step (a) contain a detectable amount of the conjugate in a non-peripheral region as the number of cells of the population of step (b) contain the anti-CD20 antibody-doxorubicin conjugate in a non-peripheral region; or
- (ii) the accumulation of the conjugate in a non-peripheral region of the majority of CD20-expressing cells of the population of step (a) is between 1.5-fold and 5,000-fold greater than the accumulation of the anti-CD20 antibody-doxorubicin conjugate in the majority of CD20-expressing cells of the population of step (b).

71. (Original) A method of treating a CD20-expressing cancer, comprising administering to a subject in need of such treatment an effective amount of an anti-CD20 antibody-cytotoxic agent conjugate, wherein the cytotoxic agent of the anti-CD20 antibody-cytotoxic agent conjugate has an  $IC_{50}$  of between 40-fold and 4,000-fold less than the  $IC_{50}$  of doxorubicin, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, and wherein the  $IC_{50}$  of each of the cytotoxic agent and doxorubicin is measured by a method comprising:

- (a) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of the cytotoxic agent for a 72- to 96-hour period;

- (b) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of doxorubicin for a 72- to 96-hour period; and
- (c) identifying a concentration of the cytotoxic agent and doxorubicin, respectively, at which 50% fewer cells in the CD20-expressing cell populations of steps (a) and (b), respectively, are viable at the end of the period relative to a CD20-expressing cell population cultured in the absence of the cytotoxic agent and doxorubicin,

wherein the CD20-expressing cell populations of steps (a), (b) and (c) are of the same cell type and are cultured under the same conditions,

and wherein the concentration of the cytotoxic agent and doxorubicin identified in step (c) is the  $IC_{50}$  of the cytotoxic agent and doxorubicin, respectively.

72. (Original) A method of treating a CD20-expressing cancer, comprising administering to a subject in need of such treatment an effective amount of an anti-CD20 antibody-cytotoxic agent conjugate, wherein the anti-CD20 antibody-cytotoxic agent conjugate has an  $IC_{50}$  of between 40-fold and 4,000-fold less than the  $IC_{50}$  of an anti-CD20 antibody-doxorubicin conjugate, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, and wherein the  $IC_{50}$  of each of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate is measured by a method comprising:

- (a) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of the anti-CD20 antibody-cytotoxic agent conjugate for a 72- to 96-hour period;
- (b) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of the anti-CD20 antibody-doxorubicin conjugate for a 72- to 96-hour period; and
- (c) identifying a concentration of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate, respectively, at which 50% fewer cells in the CD20-expressing cell populations of steps (a) and (b), respectively, are viable at the end of the period relative to a CD20-expressing cell population cultured in the

absence of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate,  
wherein the CD20-expressing cell populations of steps (a), (b) and (c) are of the same cell type and are cultured under the same conditions,  
and wherein the concentration of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate identified in step (c) is the IC<sub>50</sub> of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate, respectively.

73. (Original) A method of treating a CD20-expressing cancer, comprising administering to a subject in need of such treatment an effective amount of an anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate has a rate of accumulation in a CD20-expressing cell that is between 20-fold and 5,000-fold greater than the rate of accumulation of an unconjugated form of the anti-CD20 antibody in the CD20-expressing cell, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the rates of accumulation of the conjugate and of the unconjugated form of the antibody are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the unconjugated antibody, wherein the populations of steps (a) and (b) are cultured under the same conditions; and
- (c) measuring the amount of the conjugate and unconjugated antibody accumulated in the populations of steps (a) and (b), respectively.

74. (Original) A method of treating a CD20-expressing cancer, comprising administering to a subject in need of such treatment an effective amount of an anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate has a rate of accumulation in a CD20-expressing cell that is between 20-fold and 5,000-fold greater than the rate of accumulation of an anti-CD20 antibody-doxorubicin conjugate in a CD20-expressing cell of the same cell type, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, and wherein the rates of accumulation of the anti-CD20 antibody-cytotoxic agent conjugate and of the anti-CD20 antibody-doxorubicin conjugate are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-cytotoxic agent conjugate;
- (b) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-doxorubicin conjugate, wherein the populations of steps (a) and (b) are cultured under the same conditions; and
- (c) measuring the amount of the anti-CD20 antibody-cytotoxic agent conjugate and anti-CD20 antibody-doxorubicin conjugate accumulated in the populations of steps (a) and (b), respectively.

75. (Original) A method of treating a CD20-expressing cancer, comprising administering to a subject in need of such treatment an effective amount of an anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate exhibits an accumulation in a non-peripheral region inside a CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of an unconjugated form of the anti-CD20 antibody in the CD20-expressing cell, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the accumulation of the conjugate and of the unconjugated form of the antibody are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the unconjugated form of the anti-CD20 antibody; and
- (c) detecting by confocal fluorescence microscopy localization of the conjugate and the unconjugated form of the anti-CD20 antibody in the populations of steps (a) and (b), respectively,

wherein the populations of steps (a) and (b) are cultured under the same conditions and for the same period of time, and wherein the conjugate exhibits an accumulation in the CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of the unconjugated form of the anti-CD20 antibody in the CD20-expressing cell if:

- (i) between 1.5-fold and 5,000-fold as many cells of the population of step (a) contain a detectable amount of the conjugate in a non-peripheral region as the number of cells of the population of step (b) contain the unconjugated form of the antibody in a non-peripheral region; or
- (ii) the accumulation of the conjugate in a non-peripheral region of the majority of CD20-expressing cells of the population of step (a) is between 1.5-

fold and 5,000-fold greater than the accumulation of the unconjugated form of the anti-CD20 antibody in the majority of CD20-expressing cells of the population of step (b).

76. (Original) A method of treating a CD20-expressing cancer, comprising administering to a subject in need of such treatment an effective amount of an anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate exhibits an accumulation in a non-peripheral region inside a CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of an anti-CD20 antibody-doxorubicin conjugate, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, in the CD20-expressing cell, wherein the accumulation of the conjugate and of the anti-CD20 antibody-doxorubicin conjugate are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-doxorubicin conjugate; and
- (c) detecting by confocal fluorescence microscopy localization of the conjugate and the anti-CD20 antibody-doxorubicin conjugate in the populations of steps (a) and (b), respectively,

wherein the populations of steps (a) and (b) are cultured under the same conditions and for the same period of time, and wherein the conjugate exhibits an accumulation in the CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of the anti-CD20 antibody-doxorubicin conjugate in the CD20-expressing cell if:

- (i) between 1.5-fold and 5,000-fold as many cells of the population of step (a) contain a detectable amount of the conjugate in a non-peripheral region as the number of cells of the population of step (b) contain the anti-CD20 antibody-doxorubicin conjugate in a non-peripheral region; or
- (ii) the accumulation of the conjugate in a non-peripheral region of the majority of CD20-expressing cells of the population of step (a) is between 1.5-fold and 5,000-fold greater than the accumulation of the anti-CD20 antibody-doxorubicin conjugate in the majority of CD20-expressing cells of the population of step (b).

78. (Original) A method of treating an immune disorder involving CD20-expressing cells, comprising administering to a subject in need of such treatment an effective amount of an anti-CD20 antibody-cytotoxic agent conjugate, wherein the cytotoxic agent of the anti-CD20 antibody-cytotoxic agent conjugate has an  $IC_{50}$  of between 40-fold and 4,000-fold less than the  $IC_{50}$  of doxorubicin, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, and wherein the  $IC_{50}$  of each of the cytotoxic agent and doxorubicin is measured by a method comprising:

- (a) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of the cytotoxic agent for a 72- to 96-hour period;
- (b) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of doxorubicin for a 72- to 96-hour period; and
- (c) identifying a concentration of the cytotoxic agent and doxorubicin, respectively, at which 50% fewer cells in the CD20-expressing cell populations of steps (a) and (b), respectively, are viable at the end of the period relative to a CD20-expressing cell population cultured in the absence of the cytotoxic agent and doxorubicin,

wherein the CD20-expressing cell populations of steps (a), (b) and (c) are of the same cell type and are cultured under the same conditions,

and wherein the concentration of the cytotoxic agent and doxorubicin identified in step (c) is the  $IC_{50}$  of the cytotoxic agent and doxorubicin, respectively.

79. (Original) A method of treating an immune disorder involving CD20-expressing cells, comprising administering to a subject in need of such treatment an effective amount of an anti-CD20 antibody-cytotoxic agent conjugate, wherein the anti-CD20 antibody-cytotoxic agent conjugate has an  $IC_{50}$  of between 40-fold and 4,000-fold less than the  $IC_{50}$  of an anti-CD20 antibody-doxorubicin conjugate, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20

antibody, and wherein the  $IC_{50}$  of each of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate is measured by a method comprising:

- (a) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of the anti-CD20 antibody-cytotoxic agent conjugate for a 72- to 96-hour period;
- (b) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of the anti-CD20 antibody-doxorubicin conjugate for a 72- to 96-hour period; and
- (c) identifying a concentration of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate, respectively, at which 50% fewer cells in the CD20-expressing cell populations of steps (a) and (b), respectively, are viable at the end of the period relative to a CD20-expressing cell population cultured in the absence of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate,

wherein the CD20-expressing cell populations of steps (a), (b) and (c) are of the same cell type and are cultured under the same conditions,

and wherein the concentration of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate identified in step (c) is the  $IC_{50}$  of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate, respectively.

80. (Original) A method of treating an immune disorder involving CD20-expressing cells, comprising administering to a subject in need of such treatment an effective amount of an anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate has a rate of accumulation in a CD20-expressing cell that is between 20-fold and 5,000-fold greater than the rate of accumulation of an unconjugated form of the anti-CD20 antibody in the CD20-expressing cell, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, and wherein the rates of accumulation of the conjugate and of the unconjugated form of the antibody are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the unconjugated antibody, wherein the populations of steps (a) and (b) are cultured under the same conditions; and

- (c) measuring the amount of the conjugate and unconjugated antibody accumulated in the populations of steps (a) and (b), respectively.

81. (Original) A method of treating an immune disorder involving CD20-expressing cells, comprising administering to a subject in need of such treatment an effective amount of an anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate has a rate of accumulation in a CD20-expressing cell that is between 20-fold and 5,000-fold greater than the rate of accumulation of an anti-CD20 antibody-doxorubicin conjugate in a CD20-expressing cell of the same cell type, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, and wherein the rates of accumulation of the anti-CD20 antibody-cytotoxic agent conjugate and of the anti-CD20 antibody-doxorubicin conjugate are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-cytotoxic agent conjugate;
- (b) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-doxorubicin conjugate, wherein the populations of steps (a) and (b) are cultured under the same conditions; and
- (c) measuring the amount of the anti-CD20 antibody-cytotoxic agent conjugate and anti-CD20 antibody-doxorubicin conjugate accumulated in the populations of steps (a) and (b), respectively.

82. (Original) A method of treating an immune disorder involving CD20-expressing cells, comprising administering to a subject in need of such treatment an effective amount of an anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate exhibits an accumulation in a non-peripheral region inside a CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of an unconjugated form of the anti-CD20 antibody in the CD20-expressing cell, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the accumulation of the conjugate and of the unconjugated form of the antibody are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the unconjugated form of the anti-CD20 antibody; and



- (c) detecting by confocal fluorescence microscopy localization of the conjugate and the unconjugated form of the anti-CD20 antibody in the populations of steps (a) and (b), respectively,

wherein the populations of steps (a) and (b) are cultured under the same conditions and for the same period of time, and wherein the conjugate exhibits an accumulation in the CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of the unconjugated form of the anti-CD20 antibody in the CD20-expressing cell if:

- (i) between 1.5-fold and 5,000-fold as many cells of the population of step (a) contain a detectable amount of the conjugate in a non-peripheral region as the number of cells of the population of step (b) contain the unconjugated form of the antibody in a non-peripheral region; or
- (ii) the accumulation of the conjugate in a non-peripheral region of the majority of CD20-expressing cells of the population of step (a) is between 1.5-fold and 5,000-fold greater than the accumulation of the unconjugated form of the anti-CD20 antibody in the majority of CD20-expressing cells of the population of step (b).

83. (Original) A method of treating an immune disorder involving CD20-expressing cells, comprising administering to a subject in need of such treatment an effective amount of an anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate exhibits an accumulation in a non-peripheral region inside a CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of an anti-CD20 antibody-doxorubicin conjugate, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, in the CD20-expressing cell, wherein the accumulation of the conjugate and of the anti-CD20 antibody-doxorubicin conjugate are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-doxorubicin conjugate; and
- (c) detecting by confocal fluorescence microscopy localization of the conjugate and the anti-CD20 antibody-doxorubicin conjugate in the populations of steps (a) and (b), respectively,

wherein the populations of steps (a) and (b) are cultured under the same conditions and for the same period of time, and wherein the conjugate exhibits an accumulation in the CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of the anti-CD20 antibody-doxorubicin conjugate in the CD20-expressing cell if:

- (i) between 1.5-fold and 5,000-fold as many cells of the population of step (a) contain a detectable amount of the conjugate in a non-peripheral region as the number of cells of the population of step (b) contain the anti-CD20 antibody-doxorubicin conjugate in a non-peripheral region; or
- (ii) the accumulation of the conjugate in a non-peripheral region of the majority of CD20-expressing cells of the population of step (a) is between 1.5-fold and 5,000-fold greater than the accumulation of the anti-CD20 antibody-doxorubicin conjugate in the majority of CD20-expressing cells of the population of step (b).

84-95            (Canceled)

96.            (Original) A kit comprising in a first container, an anti-CD20 antibody, and in a second container, a cytotoxic agent, wherein the cytotoxic agent has an  $IC_{50}$  of between 40-fold and 4,000-fold less than the  $IC_{50}$  of doxorubicin, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, and wherein the  $IC_{50}$  of each of the cytotoxic agent and doxorubicin is measured by a method comprising:

- (a)    culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of the cytotoxic agent for a 72- to 96-hour period;
- (b)    culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of doxorubicin for a 72- to 96-hour period; and
- (c)    identifying a concentration of the cytotoxic agent and doxorubicin, respectively, at which 50% fewer cells in the CD20-expressing cell populations, respectively, are viable at the end of the period relative to a CD20-expressing cell population cultured in the absence of the cytotoxic agent and doxorubicin,

wherein the CD20-expressing cell populations of steps (a), (b) and (c) are of the same cell type and are cultured under the same conditions,  
and wherein the concentration of the cytotoxic agent and doxorubicin identified in step (c) is the IC<sub>50</sub> of the cytotoxic agent and doxorubicin, respectively.

97 (Canceled)

98. (Original) A kit comprising in a first container, an anti-CD20 antibody, and in a second container, a cytotoxic agent, wherein upon conjugation of the anti-CD20 antibody and the drug, the resulting conjugate has a rate of accumulation in a CD20-expressing cell that is between 20-fold and 5,000-fold greater than the rate of accumulation of an unconjugated form of the anti-CD20 antibody in the CD20-expressing cell, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, and wherein the rates of accumulation of the conjugate and of the unconjugated form of the antibody are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the unconjugated antibody, wherein the populations of steps (a) and (b) are cultured under the same conditions; and
- (c) measuring the amount of the conjugate and unconjugated antibody accumulated in the populations of steps (a) and (b), respectively.

99. (Original) A kit comprising in a first container, an anti-CD20 antibody, and in a second container, a cytotoxic agent, wherein upon conjugation of the anti-CD20 antibody and the drug, the resulting conjugate has a rate of accumulation in a CD20-expressing cell that is between 20-fold and 5,000-fold greater than the rate of accumulation of an anti-CD20 antibody-doxorubicin conjugate in a CD20-expressing cell of the same cell type, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, and wherein the rates of accumulation of the anti-CD20 antibody-cytotoxic agent conjugate and of the anti-CD20 antibody-doxorubicin conjugate are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-cytotoxic agent conjugate;

- (b) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-doxorubicin conjugate, wherein the populations of steps (a) and (b) are cultured under the same conditions; and
- (c) measuring the amount of the anti-CD20 antibody-cytotoxic agent conjugate and anti-CD20 antibody-doxorubicin conjugate accumulated in the populations of steps (a) and (b), respectively.

100. (Original) A kit comprising in a first container, an anti-CD20 antibody, and in a second container, a cytotoxic agent, wherein upon conjugation of the anti-CD20 antibody and the drug, the resulting conjugate exhibits an accumulation in a non-peripheral region inside a CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of an unconjugated form of the anti-CD20 antibody in the CD20-expressing cell, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the accumulation of the conjugate and of the unconjugated form of the antibody are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the unconjugated form of the anti-CD20 antibody; and
- (c) detecting by confocal fluorescence microscopy localization of the conjugate and the unconjugated form of the anti-CD20 antibody in the populations of steps (a) and (b), respectively,

wherein the populations of steps (a) and (b) are cultured under the same conditions and for the same period of time, and wherein the conjugate exhibits an accumulation in the CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of the unconjugated form of the anti-CD20 antibody in the CD20-expressing cell if:

- (i) between 1.5-fold and 5,000-fold as many cells of the population of step (a) contain a detectable amount of the conjugate in a non-peripheral region as the number of cells of the population of step (b) contain the unconjugated form of the antibody in a non-peripheral region; or
- (ii) the accumulation of the conjugate in a non-peripheral region of the majority of CD20-expressing cells of the population of step (a) is between 1.5-fold and 5,000-fold greater than the accumulation of the unconjugated form of

the anti-CD20 antibody in the majority of CD20-expressing cells of the population of step (b).

101. (Original) A kit comprising in a first container, an anti-CD20 antibody, and in a second container, a cytotoxic agent, wherein upon conjugation of the anti-CD20 antibody and the drug, the resulting conjugate exhibits an accumulation in a non-peripheral region inside a CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of an anti-CD20 antibody-doxorubicin conjugate, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, in the CD20-expressing cell, wherein the accumulation of the conjugate and of the anti-CD20 antibody-doxorubicin conjugate are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-doxorubicin conjugate; and
- (c) detecting by confocal fluorescence microscopy localization of the conjugate and the anti-CD20 antibody-doxorubicin conjugate in the populations of steps (a) and (b), respectively,

wherein the populations of steps (a) and (b) are cultured under the same conditions and for the same period of time, and wherein the conjugate exhibits an accumulation in the CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of the anti-CD20 antibody-doxorubicin conjugate in the CD20-expressing cell if:

- (i) between 1.5-fold and 5,000-fold as many cells of the population of step (a) contain a detectable amount of the conjugate in a non-peripheral region as the number of cells of the population of step (b) contain the anti-CD20 antibody-doxorubicin conjugate in a non-peripheral region; or
- (ii) the accumulation of the conjugate in a non-peripheral region of the majority of CD20-expressing cells of the population of step (a) is between 1.5-fold and 5,000-fold greater than the accumulation of the anti-CD20 antibody-doxorubicin conjugate in the majority of CD20-expressing cells of the population of step (b).

102. (Original) A kit comprising in a first container, an anti-CD20 antibody, in a second container, a cytotoxic agent, and in a third container, a linker for conjugating the anti-CD20 antibody to the cytotoxic agent, wherein upon conjugation of the anti-CD20 antibody and the drug via the linker, the resulting conjugate has a rate of accumulation in a CD20-expressing cell that is between 20-fold and 5,000-fold greater than the rate of accumulation of an unconjugated form of the anti-CD20 antibody in the CD20-expressing cell, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, and wherein the rates of accumulation of the conjugate and of the unconjugated form of the antibody are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the unconjugated antibody, wherein the populations of steps (a) and (b) are cultured under the same conditions; and
- (c) measuring the amount of the conjugate and unconjugated antibody accumulated in the populations of steps (a) and (b), respectively.

103. (Original) A kit comprising in a first container, an anti-CD20 antibody, in a second container, a cytotoxic agent, and in a third container, a linker for conjugating the anti-CD20 antibody to the cytotoxic agent, wherein upon conjugation of the anti-CD20 antibody and the drug via the linker, the resulting conjugate exhibits an accumulation in a non-peripheral region inside a CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of an unconjugated form of the anti-CD20 antibody in the CD20-expressing cell, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the accumulation of the conjugate and of the unconjugated form of the antibody are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the unconjugated form of the anti-CD20 antibody; and
- (c) detecting by confocal fluorescence microscopy localization of the conjugate and the unconjugated form of the anti-CD20 antibody in the populations of steps (a) and (b), respectively,

wherein the populations of steps (a) and (b) are cultured under the same conditions and for the same period of time, and wherein the conjugate exhibits an accumulation in the CD20-expressing cell that is between 1.5-fold and 5,000-fold greater

than the accumulation of the unconjugated form of the anti-CD20 antibody in the CD20-expressing cell if:

- (i) between 1.5-fold and 5,000-fold as many cells of the population of step (a) contain a detectable amount of the conjugate in a non-peripheral region as the number of cells of the population of step (b) contain the unconjugated form of the antibody in a non-peripheral region; or
- (ii) the accumulation of the conjugate in a non-peripheral region of the majority of CD20-expressing cells of the population of step (a) is between 1.5-fold and 5,000-fold greater than the accumulation of the unconjugated form of the anti-CD20 antibody in the majority of CD20-expressing cells of the population of step (b).

104. (Original) A kit comprising in a first container, an anti-CD20 antibody, in a second container, a cytotoxic agent, and in a third container, a linker for conjugating the anti-CD20 antibody to the cytotoxic agent, wherein upon conjugation of the anti-CD20 antibody and the drug via the linker, the resulting conjugate exhibits an accumulation in a non-peripheral region inside a CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of an anti-CD20 antibody-doxorubicin conjugate, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, in the CD20-expressing cell, wherein the accumulation of the conjugate and of the anti-CD20 antibody-doxorubicin conjugate are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the conjugate;
- (b) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-doxorubicin conjugate; and
- (c) detecting by confocal fluorescence microscopy localization of the conjugate and the anti-CD20 antibody-doxorubicin conjugate in the populations of steps (a) and (b), respectively,

wherein the populations of steps (a) and (b) are cultured under the same conditions and for the same period of time, and wherein the conjugate exhibits an accumulation in the CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of the anti-CD20 antibody-doxorubicin conjugate in the CD20-expressing cell if:

- (i) between 1.5-fold and 5,000-fold as many cells of the population of step (a) contain a detectable amount of the conjugate in a non-peripheral region as the number of cells of the population of step (b) contain the anti-CD20 antibody-doxorubicin conjugate in a non-peripheral region; or
- (ii) the accumulation of the conjugate in a non-peripheral region of the majority of CD20-expressing cells of the population of step (a) is between 1.5-fold and 5,000-fold greater than the accumulation of the anti-CD20 antibody-doxorubicin conjugate in the majority of CD20-expressing cells of the population of step (b).

105. (Original) A kit comprising in a first container, an anti-CD20 antibody, in a second container, a cytotoxic agent, and in a third container, a linker for conjugating the anti-CD20 antibody to the cytotoxic agent, wherein upon conjugation of the anti-CD20 antibody and the drug via the linker, the resulting conjugate has a rate of accumulation in a CD20-expressing cell that is between 20-fold and 5,000-fold greater than the rate of accumulation of an anti-CD20 antibody-doxorubicin conjugate in a CD20-expressing cell of the same cell type, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, and wherein the rates of accumulation of the anti-CD20 antibody-cytotoxic agent conjugate and of the anti-CD20 antibody-doxorubicin conjugate are measured by a method comprising:

- (a) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-cytotoxic agent conjugate;
- (b) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-doxorubicin conjugate, wherein the populations of steps (a) and (b) are cultured under the same conditions; and
- (c) measuring the amount of the anti-CD20 antibody-cytotoxic agent conjugate and anti-CD20 antibody-doxorubicin conjugate accumulated in the populations of steps (a) and (b), respectively.

106. (Original) A kit comprising:

- (a) an anti-CD20 antibody-cytotoxic agent conjugate, wherein the cytotoxic agent of the anti-CD20 antibody-cytotoxic agent conjugate has an  $IC_{50}$  of between 40-fold and 4,000-fold less than the  $IC_{50}$  of



doxorubicin, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, and wherein the  $IC_{50}$  of each of the cytotoxic agent and doxorubicin is measured by a method comprising:

- (i) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of the cytotoxic agent for a 72- to 96-hour period;
- (ii) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of doxorubicin for a 72- to 96-hour period; and
- (iii) identifying a concentration of the cytotoxic agent and doxorubicin, respectively, at which 50% fewer cells in the CD20-expressing cell populations of steps (i) and (ii), respectively, are viable at the end of the period relative to a CD20-expressing cell population cultured in the absence of the cytotoxic agent and doxorubicin,

wherein the CD20-expressing cell populations of steps (i), (ii) and (iii) are of the same cell type and are cultured under the same conditions,

and wherein the concentration of the cytotoxic agent and doxorubicin identified in step (iii) is the  $IC_{50}$  of the cytotoxic agent and doxorubicin, respectively, and

- (b) a notice by a regulatory agency indicating approval for manufacture, use or sale of the conjugate for human administration.

107. (Original) A kit comprising:

- (a) an anti-CD20 antibody-cytotoxic agent conjugate, wherein the anti-CD20 antibody-cytotoxic agent conjugate has an  $IC_{50}$  of between 40-fold and 4,000-fold less than the  $IC_{50}$  of an anti-CD20 antibody-doxorubicin conjugate, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, and wherein the  $IC_{50}$  of each of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate is measured by a method comprising:

- (i) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of the anti-CD20 antibody-cytotoxic agent conjugate for a 72- to 96-hour period;
- (ii) culturing one or more CD20-expressing cell populations in the presence of one or more concentrations of the anti-CD20 antibody-doxorubicin conjugate for a 72- to 96-hour period; and
- (iii) identifying a concentration of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate, respectively, at which 50% fewer cells in the CD20-expressing cell populations of steps (i) and (ii), respectively, are viable at the end of the period relative to a CD20-expressing cell population cultured in the absence of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate,

wherein the CD20-expressing cell populations of steps (i), (ii) and (iii) are of the same cell type and are cultured under the same conditions,

and wherein the concentration of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate identified in step (iii) is the IC<sub>50</sub> of the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate, respectively; and

- (b) a notice by a regulatory agency indicating approval for manufacture, use or sale of the conjugate for human administration.

108. (Original) A kit comprising:

- (a) an anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate has a rate of accumulation in a CD20-expressing cell that is between 20-fold and 5,000-fold greater than the rate of accumulation of an unconjugated form of the anti-CD20 antibody in the CD20-expressing cell, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, and wherein the rates of accumulation of the conjugate and of the unconjugated form of the antibody are measured by a method comprising:

- (i) culturing a population of the CD20-expressing cell with the conjugate;
  - (ii) culturing a population of the CD20-expressing cell with the unconjugated antibody, wherein the populations of steps (i) and (ii) are cultured under the same conditions; and
  - (iii) measuring the amount of the conjugate and unconjugated antibody accumulated in the populations of steps (i) and (ii), respectively; and
- (b) a notice by a regulatory agency indicating approval for manufacture, use or sale of the conjugate for human administration.

109. (Original) A kit comprising:

- (a) an anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate has a rate of accumulation in a CD20-expressing cell that is between 20-fold and 5,000-fold greater than the rate of accumulation of an anti-CD20 antibody-doxorubicin conjugate in a CD20-expressing cell of the same cell type, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, and wherein the rates of accumulation of the anti-CD20 antibody-cytotoxic agent conjugate and of the anti-CD20 antibody-doxorubicin conjugate are measured by a method comprising:
  - (i) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-cytotoxic agent conjugate;
  - (ii) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-doxorubicin conjugate, wherein the populations of steps (i) and (ii) are cultured under the same conditions; and
  - (iii) measuring the amount of the anti-CD20 antibody-cytotoxic agent conjugate and anti-CD20 antibody-doxorubicin conjugate accumulated in the populations of steps (i) and (ii), respectively; and

- (b) a notice by a regulatory agency indicating approval for manufacture, use or sale of the conjugate for human administration.

110. (Original) A kit comprising:

- (a) an anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate exhibits an accumulation in a non-peripheral region inside a CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of an unconjugated form of the anti-CD20 antibody in the CD20-expressing cell, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the accumulation of the conjugate and of the unconjugated form of the antibody are measured by a method comprising:
  - (i) culturing a population of the CD20-expressing cell with the conjugate;
  - (ii) culturing a population of the CD20-expressing cell with the unconjugated form of the anti-CD20 antibody; and
  - (iii) detecting by confocal fluorescence microscopy localization of the conjugate and the unconjugated form of the anti-CD20 antibody in the populations of steps (a) and (b), respectively,

wherein the populations of steps (a) and (b) are cultured under the same conditions and for the same period of time, and wherein the conjugate exhibits an accumulation in the CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of the unconjugated form of the anti-CD20 antibody in the CD20-expressing cell if:

- (A) between 1.5-fold and 5,000-fold as many cells of the population of step (a) contain a detectable amount of the conjugate in a non-peripheral region as the number of cells of the population of step (b) contain the unconjugated form of the antibody in a non-peripheral region; or
- (B) the accumulation of the conjugate in a non-peripheral region of the majority of CD20-expressing cells of the population of step (a) is between 1.5-fold and 5,000-fold greater than the accumulation of the unconjugated form of the

anti-CD20 antibody in the majority of CD20-expressing cells of the population of step (ii); and

- (b) a notice by a regulatory agency indicating approval for manufacture, use or sale of the conjugate for human administration.

111. (Original) A kit comprising:

- (a) an anti-CD20 antibody-cytotoxic agent conjugate, wherein the conjugate exhibits an accumulation in a non-peripheral region inside a CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of an anti-CD20 antibody-doxorubicin conjugate, with the proviso that the cytotoxic agent is not a radioisotope or a toxin, wherein the anti-CD20 antibody-cytotoxic agent conjugate and the anti-CD20 antibody-doxorubicin conjugate comprise the same anti-CD20 antibody, in the CD20-expressing cell, wherein the accumulation of the conjugate and of the anti-CD20 antibody-doxorubicin conjugate are measured by a method comprising:
  - (i) culturing a population of the CD20-expressing cell with the conjugate;
  - (ii) culturing a population of the CD20-expressing cell with the anti-CD20 antibody-doxorubicin conjugate; and
  - (iii) detecting by confocal fluorescence microscopy localization of the conjugate and the anti-CD20 antibody-doxorubicin conjugate in the populations of steps (a) and (b), respectively,

wherein the populations of steps (a) and (b) are cultured under the same conditions and for the same period of time, and wherein the conjugate exhibits an accumulation in the CD20-expressing cell that is between 1.5-fold and 5,000-fold greater than the accumulation of the anti-CD20 antibody-doxorubicin conjugate in the CD20-expressing cell if:

(A) between 1.5-fold and 5,000-fold as many cells of the population of step (a) contain a detectable amount of the conjugate in a non-peripheral region as the number of cells of the population of step (b) contain the anti-CD20 antibody-doxorubicin conjugate in a non-peripheral region; or

- (B) the accumulation of the conjugate in a non-peripheral region of the majority of CD20-expressing cells of the population of step (a) is between 1.5-fold and 5,000-fold greater than the accumulation of the anti-CD20 antibody-doxorubicin conjugate in the majority of CD20-expressing cells of the population of step (ii); and
- (b) a notice by a regulatory agency indicating approval for manufacture, use or sale of the conjugate for human administration.

112-121

(Canceled)